Regional wall mechanics and blunt traumatic aortic rupture at the isthmus

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Abstract

Objective: Blunt traumatic aortic injury (BTAI) is part of a spectrum of diseases termed acute aortic syndrome that accounts for 20% of road traffic accident related deaths. The injury has a complex aetiology with a number of putative mechanisms accounting for the injury profile, characteristics of which include a transverse primary intimal tear located at the aortic isthmus. We hypothesised that an understanding of regional aortic wall mechanics would contribute to an understanding of the aetiology of BTAI. Methods: Samples of porcine aorta were prepared from ascending (A), descending (D) and peri-isthmus regions (I). A histological analysis of aortic wall architecture was performed at the site of attachment of the ligamentum arteriosum. Samples were mounted in a bubble inflation clamping rig, connected via a solenoid release valve to a compressed air reservoir. Using a pressure transducer and high-speed camera (1000 fps) we collected data on wall thickness, rupture pressure and radial extension, allowing calculation of ultimate tensile stress. Results: Histological analysis at the point of attachment of the ligamentum arteriosum to the isthmus shows some heterogeneity in cellular architecture extending deep into the tunica media. Wall thickness was significantly different between the three sampled regions (A > I > D, p < 0.05). However, we found no difference in absolute rupture pressure between the three regions (kPa), (A, 300 ± 28.9; I, 287 ± 48.3; D, 321 ± 29.6). Radial extension (cm) was significantly greater in A vs I (p < 0.05), (A, 1.85 ± 0.114; I, 1.66 ± 0.109; D, 1.70 ± 0.138). Ultimate tensile stress (kPa), (A, 3699 ± 789; I, 3248 ± 1430; D, 4260 ± 1626) was significantly greater in D than I (p < 0.05). Conclusions: The mechanism of blunt traumatic aortic rupture is not mechanically simple but must correspond to a complex combination of both relative motion of the structures within the thorax and local loading of the tissues, either as a result of their anatomy or due to the nature of the impact. A pressure spike alone is unlikely to be the primary cause of the peri-isthmus injury but may well be a contributory prerequisite.

1. Introduction

Aortic rupture is the second most common cause of death following vehicle-related blunt trauma, exceeded only by head injury [1]. We have previously published an analysis of the UK-based Co-operative Crash Injury Study [2], a detailed database of vehicle related injury, indicating that blunt aortic trauma accounts for approximately 20% of vehicle related deaths. The literature [3] describes a scene survival of approximately 5% suggesting most victims sustain immediate and catastrophic aortic failure with exsanguination and death at the site of trauma; so-called blunt traumatic aortic rupture (BTAR). A small number of victims sustain a lesser partial mural injury that allows transfer to hospital and definitive treatment; so-called blunt traumatic aortic injury (BTAI). The incidence of BTAI/R is unknown in the United Kingdom, however estimates of 7500–8000 deaths per year have been reported in USA and Canada [4].

Aortic injury is now considered as part of a spectrum of diseases (acute aortic syndrome), with blunt aortic trauma being at one end of the disease continuum, and including other process such as classical dissection, intimal flap, sub-intimal haematoma, intra-mural haematoma, penetrating atherosclerotic ulcer, through BTAI to BTAR [5]. While the characteristics of BTAI/R have been well documented, including the circumstances under which it occurs, the transduction of impact energy through the thorax, and the evolution of the injury to the aortic wall, the exact aetiology that accounts for injury characteristics remains unclear [6]. In particular, it is uncertain why despite a range of trauma...
scenarios, the injury profiles of victims are very similar with the majority being transverse primary intimal tears occurring in the peri-isthmus region [3]. Several hypotheses have been put forward to account for the transverse primary intimal nature of these injuries, which broadly centre on a variable contribution from mechanical deformation and intraluminal hypertension [7]. Clearly, for the anatomic location of injury to be so consistent between individuals and trauma scenarios one may speculate that there is a feature of the geometry of the aorta, or an area of focal weakness that leads to an injury focus at the isthmus. We have chosen to investigate the latter by hypothesising that there are regional differences in the mechanical properties of the aortic wall that would lead to focal injuries at the isthmus.

2. Methods

2.1. Animal husbandry and specimen preparation

Fresh porcine (Sus scrofa domestica) aorta was obtained from the abattoir. A random mixture of male and female pigs, aged 10—12 months, were selected for tissue sampling. All pigs were reared and slaughtered humanely according to Department of Environment, Food and Rural Affairs (DEFRA, UK). These animals were not bred specifically for research. Each aorta was dissected into three test regions; the ascending (A), isthmus (I) and descending (D) aorta. Each region was cut longitudinally and the wall thickness measured with vernier calipers.

2.2. Histological measurements

Samples were fixed in 10% formalin for 48 h (Sigma—Aldrich, Gillingham, UK) and processed into paraffin wax. Eight micrometer sections were cut using a rotary microtome (Micron HM 325, MICROM Laborgerate GmbH, Walldorf, Germany) and stained with Weigert’s resorcin fuchsin and counterstained with sirius red [8]. Samples were viewed with a Nikon Eclipse TS100 (Nikon Corporation, Tokyo, Japan) microscope and pictures were taken using a Nikon Digital Sight, DS-5M-L1 (Nikon Corporation, Tokyo, Japan) camera.

2.3. Biomechanical measurements

A rig was constructed as described by Mohan and Melvin [9]. Samples were mounted in a bubble inflation clamping rig using an O-ring and Loctite super glue (Henkel Technologies, Dusseldorf, Germany). Each aortic sample was stamped with an inked circular grid. The isthmus specimen was always placed with the trimmed remnant of the ligamentum arteriosum in the centre of the innermost circle on the inked circular grid (Fig. 1). The bubble inflation clamping rig, with the aortic specimen window, was connected via a solenoid release valve to a compressed air reservoir. Pressure was measured using a transducer and amplifier, the signal being recorded by a data logger using Spike2™ software (Cambridge Electronic Design Limited). The camera simultaneously recorded a plan view and a profile view (via mirrors mounted at 45°). The compressed air reservoir was charged and when the solenoid valve was triggered the camera (1000 fps) commenced recording (Fig. 2a). (The high speed camera was a Kodak Motion Corder analyzer model SR, Eastman Kodak, San Diego, CA.). Simultaneously, the data logger recorded the output from the amplified pressure transducer.

Two specimen modes of failure were used as data exclusion criteria. These were the specimen edge slipping out of the bubble inflation clamping rig prior to rupture (due to insufficient clamping or glue failure) and the aorta specimen rupturing at the clamped rim. The image that preceded the rupture was used to calculate radial extension and hoop stress that provided values to calculate ultimate tensile stress (Fig. 2b). Experiments were conducted until we had data from all three regions for 10 individuals.

2.4. Derived values

The variables: rupture pressure, $P$; initial membrane thickness, $h_0$; initial innermost circle diameter, $d_0$; diameter of innermost circle in frame prior to rupture, $d$; and radius of curvature of deformed aorta specimen in frame prior to rupture, $R$ were recorded. These variables were input to define values for ultimate tensile stress, calculated from values for radial extension and hoop stress.

$$\lambda = \frac{d}{d_0}$$  
$$s_E = \frac{PR}{2h_0}$$  
$$\sigma_E = \sigma_E \times \lambda^2$$

2.5. Statistical analysis

The outcome parameters for this study (e.g. ultimate tensile stress) are quantitative, but not necessarily normally distributed. We therefore chose to test our initial hypothesis that the isthmus region is inherently different from the others by comparing it with adjacent regions using the robust
non-parametric Wilcoxon matched pairs signed ranks test (2-tailed at a significance level of $p = 0.05$). This test allows us to increase the sensitivity of our analysis by exploiting the fact that the results could be paired. Similarly, median values and quartiles were calculated to provide summary statistical information. SPSS 10.0.5 for Windows, SPSS Inc. Chicago, Illinois was used for all statistical analysis.

3. Results

3.1. Macroscopic measurements

The median wall thickness increased through sequence; descending, isthmus and ascending aorta regions. The isthmus region was statistically thicker than the descending aorta and less thick than the ascending (Fig. 3A), however, there was considerable overlap between the regions.

3.2. Histological measurements

We examined the three aorta regions histologically. The Weigert’s elastin resourcin and sirius red differentiated between the elastin and collagen fibres. These fibres are known to have different mechanical properties, with collagen’s Young’s modulus being greater than elastin; the greater the collagen to elastin ratio the lower the extension to rupture. The ligament ductus arteriosus, has a high collagen content giving rise to the relatively inelastic properties of ligament (Fig. 4A). There is a transitional zone between the ligament and the aorta’s adventitia/media (Fig. 4B). The media and intima layers of the aorta are predominantly composed of elastin (Fig. 4C and D). Fig. 5 shows the region where the aorta wall has fused (ductus arteriosus). Note the incomplete integration of the elastin fibres.

3.3. Biomechanical measurements

Our hypothesis that the highly specific regional localisation of BTAR is due to the mechanical properties of the aortic
The wall at the isthmus implies that there will be little, if any, overlap in the values between the isthmus and adjacent regions. An immediate inspection of Fig. 3 shows that there is considerable overlap in all parameters.

While there is a statistically significant difference in wall thickness between the regions (A > I > D, \( p < 0.05 \)), there is no such difference in rupture pressure (kPa), (A, 300 ± 28.9; I, 287 ± 48.3; D, 321 ± 29.6), with all median rupture pressures being within 7% of each other (Fig. 3B). This clearly does not correspond to the consistency with which rupture occurs at the isthmus.

The two parameters most relevant to the interpretation of failure mechanisms are radial extension to failure (radial extension (cm) was significantly greater in A vs I (\( p < 0.05 \)), (A, 1.85 ± 0.114; I, 1.66 ± 0.109; D, 1.70 ± 0.138)) and ultimate tensile stress (ultimate tensile stress (kPa), (A, 3699 ± 789; I, 3248 ± 1430; D, 4260 ± 1626) was significantly greater in D than I (\( p < 0.05 \)), (Fig. 3C). The former is important when considering mechanisms by which the aorta is defined by a prescribed motion, while the latter is important when loading is by an external force or pressure. In both cases, the isthmus region was found to be the most vulnerable in terms of median value, but statistically significant differences were found between the isthmus and only one adjacent region. Certainly the degree of overlap between the isthmus and the adjacent regions, both within individuals and between individuals, was large. It is therefore highly unlikely that the degree of mechanical vulnerability of the isthmus region due to its intrinsic mechanical properties accounts for the clinical observation that failure normally occurs at this site.

4. Discussion

The exact aetiology of blunt traumatic aortic rupture has remained elusive, with the large number of putative mechanisms described in the literature being testimony to this fact. At the centre of the controversy is a desire to explain the injury profile of BTAR which typically occurs at the isthmus as a transverse tear initiated in the intimal layer [3]. To date, all the hypotheses around blunt trauma and aortic injury are based on a variable contribution from: (a) mechanical deformation, (b) intraluminal hypertension and (c) mechanical characteristics of the aortic wall [7]. The exact process by which some or all of these mechanisms are channelled through a final common pathway to cause consistent primary transverse intimal injury to the isthmus, despite a wide range of trauma scenarios, remains unknown.

5. Mechanisms of injury

5.1. Mechanical deformation

Mechanical deformation (i.e. tension, torsion, bending or shear) causing injury of the peri-isthmus aorta during trauma may occur by a number of mechanisms [10]. Accepted dogma at the centre of many of these mechanisms is the suggestion that the descending aorta is fixed to the spine by mediastinal pleura relative to the more mobile arch and ascending aorta resulting in a foci of stress at the isthmus [11—13]. This belief lies at the basis of the shovelling effect [14] in which the heart and aortic arch are displaced upwards following trauma, while the descending aorta is tethered to the spine and fixed, resulting in stress at the isthmus. A second hypothesis based on a relatively fixed descending aorta has been suggested by Siegel et al. [15], as part of the CIREN Study. These authors suggest that the intrathoracic aorta becomes suprapressurised following lateral impact causing it to behave as a rigid lever system. The long arm of the lever is thought to be the proximal aorta and the short arm is suggested to be the isthmus, fixed distally at the descending aorta. With the left subclavian artery acting as the fulcrum it is conceivable that impact forces may be magnified at the isthmus by an Archimedes effect. In addition, the vestigial ligamentum arteriosum, between the pulmonary artery and isthmus is thought to create an anchor point and focus of stress in this area. A novel mode of disruption has been suggested by Crass et al. [16]; the so-called osseous pinch hypothesis which suggests a mechanical force on the aorta, through entrapment between the manubrium, first rib, clavicles and vertebral bodies following trauma, contributes to stress at the isthmus.
5.2. Intra-luminal hypertension

A number of mechanisms may contribute to intra-luminal hypertension, either singularly or in combination as a resonant effect. A simple intravascular pressure spike secondary to chest compression was the first and most simple hypothesis [17,18]. However, pressures in excess of 2500 mmHg (330 kPa) are required to rupture the aorta under experimental conditions, and this has resulted in a number of more complex putative mechanisms that might contribute in causing such a pressure surge [7]. The waterhammer hypothesis [19] suggests that blunt trauma causes occlusion of the diaphragmatic orifice through which the thoracic aorta passes, resulting in a reflected intraluminal pressure wave causing maximum affect at the arch. Vessel occlusion in the thoracic inlet (osseous pinch) and mediastinal displacement (shovelling effect) will contribute to a magnification of the pressure wave. Other physiological factors that might contribute to hypertension include the cardiopulmonary dynamic at the time of impact, a catecholamine surge associated with the flight or fight response and the biphasic pressure wave of the Valsalva effect during anticipated impact [20].

5.3. Biomechanical characteristics of the aortic wall

Detailed biomechanical experimentation has provided some insight into the injury profile of this condition [9,21,22]. Early investigators excluded a sudden rise in pressure as a cause for BTAR rationalising that if the aorta were an isotropic cylindrical vessel under pressure it would rupture axially rather than transversely. However, tensile tests by Shah et al. [21], Mohan and Melvin [9] and Yamada [22] and have shown that the aorta is anisotropic with greater stiffness in the circumferential direction. Because ultimate tensile strength in the transverse direction is approximately twice that in the longitudinal direction rupture may well occur transversely following a simple pressure spike. These authors point out that the scenario is further complicated by the fact that the aorta is unlikely to be perfect cylinder during blunt trauma and this may be contributory in the observed transverse tear. Interestingly, work by Zhao et al. [10] using FE modelling based on data from Holzapfel [23] have shown that the tunica intima is relatively stiffer than the tunica media and adventitia, acting as a focus of stress during a given pressure and suggesting this accounts for the primary intimal tear seen with this injury. Other on-going work using finite element analysis of a three layer aortic wall model to study the effect of mechanical deformation has suggested that bending, stretching and torsion produce an expected preferential intimal stress consistent with the observation that this is typically an inside out injury [24].

6. Peri-isthmus biomechanics

An accepted criticism underpinning much of this work has been a lack of comparative data on regional aortic wall mechanics and the contribution of any putative heterogeneity to the resulting peri-isthmus injury. We hypothesised that this injury is due to a focal vulnerability due to regional variation in aortic wall properties. We expected that in testing this hypothesis we would provide a better understanding of the relative contributon of intraluminal hypertension, mechanical deformation and aortic wall biomechanics, to the aetiology of blunt traumatic aortic rupture. Our results show that for all parameters there is considerable overlap in properties between the isthmus and the adjacent regions (Fig. 3). In many cases, we were unable to find statistically significant differences with a sample size of 10 individuals and matching results by individual. Further, since these were pigs of similar age and size at slaughter, we would expect the results to be less variable between individuals than a human population. We are therefore able to reject our initial hypothesis that BTAR normally occurs at the isthmus due to the intrinsic mechanical properties of the aortic wall. Clearly, the explanation for injury localisation is more complex.

We were able to find some minor differences in the properties of the aortic wall between the isthmus and the adjacent regions. The isthmus showed less extension to failure than the ascending aorta, which may be significant in mechanisms where an applied deformation is the dominant loading. Similarly, the isthmus showed a lower ultimate tensile stress than the descending aorta, which might contribute to a failure mechanism where forces (or intralumenal pressures) are the dominant form of loading. We conclude from this that intraluminal hypertension as a univariate mechanism, either due to cardiovascular compression, catecholamine surge or a Valsalva effect, are not responsible for BTAR localised to the isthmus. Were this the case, we would expect BTAR to be randomly distributed throughout the aorta. The waterhammer effect, as a cause for intraluminal hypertension relies on a more sophisticated mechanism with an intraluminal pressure spike reflected from the diaphragm and exerting its maximum effect at the curvature around the isthmus. This mechanism of intraluminal hypertension has spatial and temporal aspects that our experiments are not designed to examine. Localised peri-isthmus loading as a result of a resonant waterhammer type effect, superimposed on mechanical loading seems a more plausible mechanism.

7. Peri-isthmus histology

Our histological analysis in porcine samples of the peri-isthmus region has demonstrated heterogeneity in the aortic wall at the site of attachment of the ligamentum arteriosum. We are not aware of the publication of such data in porcine tissue. There appears to be obvious lines of demarcation at this site with a suggestion of greater collagen fibre density in this region. Despite this observation, there was no translation of structural heterogeneity into functional heterogeneity, despite our experimental protocol to position the ligamentum arteriosum in the centre of the mounted sample. This excludes the possibility that the isthmus is simply inherently weaker than other regions of the aortic wall; however it does not allow us to comment on the effect of any relative motion about the isthmus through differential movement of the pulmonary artery and aorta.
8. Application of results

We have presented the results of simple experiments to determine the properties of the entire porcine aortic wall in peri-isthmus region. These results are an important component in understanding the mechanisms of BTAR, however they must be applied within the context of the different mechanisms rather than be treated in isolation:

1. This experiment is designed to quantify the properties of the arterial wall rather than to reproduce the complex geometry of an aorta in vivo. This work does not reproduce the sequence of events that may be expected following trauma to the chest. In particular, and as pointed out by Mohan and Melvin [9], the aorta is not a perfect cylinder and will deform non-uniformly during trauma. Regional rupture pressures in the peri-isthmus area may well be different when selected areas are placed under the additional stress transmitted through the aortic wall, conditions which our experiments were not designed to reproduce. We have previously published a finite element model of the thorax and its contents during trauma in an attempt to simulate the behaviour of the aorta within the context of the thorax, however the approach was of limited value [6].

2. In reality, the aorta has three layers (tunica intima, media and adventitia) with distinct architectural features and biomechanical properties [10,23]. At physiological levels of stress it is the tunica media that assumes importance, while at supraphysiological loading it is the tunica adventitia which is load bearing. In addition, the tunica intima is the stiffest layer suggesting why this is the site of common initial injury. This complex architecture has been validated and studied within a three layer finite element model of the aorta [10]. Our experiments evaluate the aggregated properties of all three layers at supraphysiological loading.

3. This is a model of immediate and catastrophic wall rupture which commonly follows high impact trauma (BTAR) and results in death at the scene. However, following low impact trauma the aorta may suffer a lesser partial mural injury including sub-intimal or intramural haematoma [5]. Our tests were designed to always result in complete rupture of the aortic wall, and therefore our results are applicable only to BTAR rather than a lesser partial injury.

4. Clearly this study is limited by the use of porcine aortic material as a model for human tissue. However, we would suggest that it is a better model for BTAR than material derived from human cadavers. Individuals suffering from BTAR as a result of RTA are usually young and otherwise healthy. Cadaveric tissue on the other hand is normally derived from elderly individuals that frequently have had a history of cardiovascular disease. We are unaware of any evidence that the porcine aorta has significant structural or anatomical differences compared to the human. Porcine aortas have the advantage that they are healthy and come from individuals of consistent age and size. Therefore, in the absence of data derived from young healthy aortas and evidence of structural dissimilarity between the two species that our porcine results are as close to the clinically relevant case as can be achieved.

9. Conclusion

The mechanism of BTAR is not mechanically simple but must correspond to a complex combination of both relative motion of the structures within the thorax and local loading of the tissues either as a result of their anatomy or due to the nature of the impact. A pressure spike alone is unlikely to be the primary cause of the peri-isthmus injury but may well be a contributory prerequisite.


